THE DRUG REVIEW PROCESS IN B.C. — DETAILED

PURPOSE

PharmaCare covers drugs that:

- support the health and well-being of British Columbians; and
- provide value for money.

Before PharmaCare decides to cover a drug, it undergoes a thorough review to determine whether it meets the above requirements. The review process ensures that PharmaCare coverage remains fair, effective, and sustainable.

The **FORMULARY** is the list of drugs that PharmaCare covers. To find out whether a drug is covered, use the Formulary Search.

NEW PATENTED DRUGS include new chemical and biologic entities (e.g., new antibiotics); new combination drugs (new combinations of already-approved drugs); biosimilars (biologically created drugs that are very close, but not exact, copies of another biologic drug); and new indications (new uses) for existing drugs.

GENERIC DRUGS are copies of a brand name drug. Copies can be made by other manufacturers once the patent period ends. The generic must contain the same active ingredients and work the same way as the brand name drug. Only the non-active ingredients (such as the coating for a pill) can change. Generic drugs are usually cheaper than brand name drugs because they cost less to develop and there is competition between the companies that make them. Generic drugs still have to get approval by Health Canada before they can be sold.

DRUG REVIEW PROCESSES FOR NEW PATENTED DRUGS

In Canada, the drug review process takes place in three stages.

STAGE 1 – FEDERAL GOVERNMENT – HEALTH CANADA

All patented and generic drugs sold in Canada require a Health Canada Notice of Compliance (NOC). Before issuing an NOC, Health Canada reviews the:

- drug's safety; and
- effect of the drug, usually compared to taking no drug at all; and
- quality of the manufacturing process used to make the drug.

>>> To learn more, see *Health Canada drug review process*.

STAGE 2 – NATIONAL REVIEW – COMMON DRUG REVIEW

To have their patented drugs covered by public drug plans, drug submission sponsors (often a drug manufacturer) must send a submission to the Canadian Agency for Drugs and Technologies in Health (CADTH) Common Drug Review (CDR)[1]. Drug sponsors must submit applications for all:

- new chemical and biologic entities (i.e., a totally new drug or a drug that is patented in other countries but is new to Canada);
- new combination drugs (i.e., new combinations of already-approved drugs); and
- new indications (i.e., new uses for an already-reviewed drug).

Because biosimilars and generic drugs are similar to already-reviewed

[1] Quebec does not participate in the CDR process and instead uses a different drug review process.

patented drugs, they do not have to be reviewed by the CDR.

COMMON DRUG REVIEW PROCESS

The CDR process involves a review of:

- how well the drug works when compared to similar drugs that are used to treat the same condition; and
- whether the drug provides value for money.

The CDR assembles a team of independent experts to review each drug submission. The CDR team reviews patient input and prepares clinical and pharmacoeconomic evidence reports. The review findings and related input and reports are forwarded to the Canadian Drug Expert Committee (CDEC)[2], an advisory body to CADTH. CDEC reviews the findings and issues a recommendation as to whether provincial plans should cover the drug – and reasons for its recommendation – to the participating drug plans.

CDEC makes one of the following recommendations:

- reimburse (i.e., cover the drug);
- reimburse with clinical criteria and/or condition(s) (i.e., cover the drug only for patients who meet certain criteria and/or under certain conditions); and
- do not reimburse (i.e., do not cover the drug).

>>> *To learn more, see CADTH Common Drug Review.*

>>> *To learn more about drugs that are open to patient input, visit CADTH CDR patient input.*

pan-CANADIAN PHARMACEUTICAL ALLIANCE PROCESS

The Ministry may engage in national negotiations with a drug submission sponsor through the pan-Canadian Pharmaceutical Alliance (pCPA). Provinces and territories that participate in the pCPA work together to achieve greater value for brand and generic products for publically funded drug programs. All brand name drugs that are reviewed by the CDR are considered for negotiation through the pCPA.

>>> *To learn more, visit pCPA.*

[2] CDEC is composed of individuals with expertise in drug therapy, drug evaluation and drug utilization, as well as public members who bring a lay perspective to the review.

STAGE 3 – B.C. REVIEW – MINISTRY OF HEALTH PHARMACARE DRUG REVIEW

BC PharmaCare conducts its own drug review, from a B.C. perspective, before making a coverage decision. This review builds on the work completed by Health Canada and at the CDR, and does not duplicate either the federal or national review processes.

BC PharmaCare carries out the review before making a drug coverage decision based on existing policies; programs; therapeutic options; Drug Review Resource Teams (DRRT) reports that include independent expert advice from clinicians, public input, and, if applicable/available, the CDR recommendation and/or the Drug Benefit Council (DBC). The DBC screens all drugs reviewed by the CDR and determines whether to conduct a full review or to accept the CDR recommendation.

THE DRUG BENEFIT COUNCIL (DBC) is an independent drug coverage advisory committee made up of nine professional members with expertise in critical appraisal, medicine, ethics, pharmacy and health economics; and three members from the public. Their role is to review drug submissions forwarded to them by the Ministry and, based on the evidence provided, make drug coverage recommendations to the Ministry.

>>> To learn more, see the DBC Terms of Reference (PDF).

3.1 – DRUG SUBMISSION RECEIVED

Drug sponsors who want PharmaCare to cover their drug submit their application to both the CDR and BC PharmaCare at the same time. By submitting an application to both the CDR and BC PharmaCare, PharmaCare can begin gathering information about a drug submission while the CDR conducts its review, rather than waiting until the CDR finalizes its drug coverage recommendation[3].

>>> To learn more, see Submitting Patented Drugs and Biosimilars.

3.2 – GATHERING INPUT FROM PATIENTS, CAREGIVERS AND PATIENT GROUPS

PharmaCare invites B.C. patients, caregivers and patient groups to submit input specific drugs under review by completing an online survey on the PharmaCare Your Voice web page.

Once the PharmaCare receives the sponsor's drug submission, it prepares questionnaires and information sheets for posting on the website. Eligible patients, caregivers and patient groups have 4 weeks to complete the online questionnaires.

To protect the respondents' privacy, input from patients and caregivers is de-identified before being included in the drug submission package for review.

>>> To learn more, visit Your Voice.

>>> To learn more and to see the number of responses to PharmaCare questionnaires about drugs, see the Quarterly Report on Completed Drug Submission Reviews (PDF).

[3] Note that the formal BC PharmaCare review does not begin until the CDR has finalized its coverage recommendation and reasons for recommendation (see step 3.6).

3.3 – DRUG BENEFIT COUNCIL SCREENING

Once the CDR review begins, the Ministry forwards the sponsor's drug submission to the DBC for an initial screening. The DBC screens each drug to determine whether or not the drug is in the same class and treats the same indication as other PharmaCare drugs, or if they are "first in class" drugs[4]. The DBC then decides whether to conduct a full review of the drug submission, or advise PharmaCare to accept the CDR final recommendation:

- if the drug is similar[5] to drugs that have already gone through a PharmaCare review, the DBC may decide to forego a full review; and
- if the drug is a first in a class of drugs – or if the DBC believes that a full review would be beneficial – they undertake that review after the CDR completes its review and a final recommendation and reasons for recommendation has been released.

The DBC informs PharmaCare of its screening decision:

- if the DBC decides to conduct a full review of the drug submission, PharmaCare sends the submission to the Drug Review Resource Committee (DRRC)(see Step 3.4 below); and
- if the DBC decides not to conduct a full review of the drug submission, PharmaCare reviews the submission internally (see Step 3.6).

3.4 – DRUG REVIEW RESOURCE COMMITTEE (DRRC)

The DRRC, a sub-committee of the DBC, establishes the review requirements, including the type of clinical reports and other inputs available and required for a review of each drug submission. The DRRC assigns expert review teams, called Drug Review Resource Teams (DRRTs), to complete the required reports for each submission.

3.5 – DRUG REVIEW RESOURCE TEAMS (DRRTs)

Each DRRT writes reports for the drug it has been assigned. These are submitted to PharmaCare and then forwarded to the DBC as part of the drug submission package.

In developing their report, a DRRT may consider clinical evidence and pharmacoeconomics (usually prepared by the CDR) and input from clinical practice reviewers (e.g., B.C. general practitioners and specialists with disease-specific expertise).

DRRTs collect input from clinical practice reviewers in the form of short reports that capture the clinical practice perspective. These reports ask clinicians to answer questions about drug-specific prescribing and the indications that a drug seeks to treat, taking into consideration the following:

- desired treatment outcome goals;
- standard treatment options (drug and non-drug) and place in therapy;
- applicability and interpretation of available clinical evidence on decision making;
- appropriate patients to receive drugs under review, potential product utilization, including off label use; and
- other clinical practice considerations deemed relevant to the drug submission review.

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[4] A "first in class" drug can be (i) a new chemical entity that works a different way than drugs previously reviewed; (ii) a new combination of existing drugs (with significantly different ingredients); (iii) an existing drug that is now being used for a new indication; or (iv) a Subsequent Entry Biologic (SEB).

[5] A "similar" drug is, for example, a drug that belongs to a previously reviewed group of drugs that work the same way and are used to treat the same indication as previously reviewed drugs.

3.6 –MINISTRY INTERNAL REVIEW

PharmaCare starts its internal review process when the patented drug has undergone the necessary Health Canada and CDR reviews, and after CDR has issued its final coverage recommendation.

If the CDR recommendation is "do not reimburse," PharmaCare typically does not forward the submission to the DBC. Instead, the drug will be reviewed by PharmaCare (see step 3.8).

PharmaCare considers whether or not to participate in pCPA negotiations, if applicable.

3.7 – DRUG BENEFIT COUNCIL REVIEW

The DBC examines all applicable CDR and DRRT reports, written comments from drug sponsors, patient input, and other relevant review documents for every drug that undergoes a full DBC review.

In reviewing the drug submission, the DBC considers:

- information on the clinical effect of the drug, and health outcomes (CDR and/or DRRT clinical evidence review reports);
- whether it is good value for British Columbians (based on CDR and/or DRRT pharmacoeconomic review reports);
- whether PharmaCare already covers any drugs that work as well as this one;
- CDR reports (if available);
- ethical considerations;
- CDR-gathered patient input;
- drug sponsor responses to the CDR Recommendation and Reasons for Recommendation; and
- public input to PharmaCare's Your Voice web page.

Based on their review, the DBC makes a recommendation to PharmaCare. The DBC recommendation and reasons for recommendation include:

- whether to cover the drug; and
- how to cover the drug (i.e., cover as a regular benefit or cover only under certain circumstances as a limited coverage drug).

>>> *To learn more, see Health Industry Professionals.*

3.8 – MINISTRY DECISION

In making any drug coverage decision, PharmaCare considers:

- existing PharmaCare policy;
- whether the drug could be covered by other programs in the Ministry;
- which PharmaCare plan(s) would cover the drug;
- whether PharmaCare has the resources to cover the cost of the drug; and
- the outcome of pCPA negotiations (if applicable).

PharmaCare may decide that the drug will be a:

- non-benefit – no coverage will be provided
- limited coverage – coverage provided based on established criteria. Pre-approval is required
- regular benefit – drug covered according to the rules of a person's PharmaCare plan, including any annual deductible requirement

PHARMACARE REVIEWS OF ALREADY-COVERED DRUGS

Drug sponsors may request changes in coverage for drugs that PharmaCare already covers, such as:

- coverage of new strengths of a drug (known as "line extensions"); or
- changes in the way that PharmaCare covers the drug (such as modification of current coverage criteria) for drugs that the CDR has not reviewed. For example, the sponsor may ask that a limited coverage drug for which patients must meet specific clinical criteria to receive coverage be changed to regular benefit.

PharmaCare reviews sponsor submissions for line extensions. PharmaCare usually forwards sponsor submissions for modifications to coverage criteria to the DBC for review and recommendations before making its decision.

If a drug has already been reviewed by the CDR, the CDR would need to review any changes to drug coverage before PharmaCare would initiate a review.

DRUG SPONSOR ENGAGEMENT DURING A REVIEW

PharmaCare provides drug submission sponsors with opportunities to engage in the review process and to respond to the PharmaCare coverage decision.

Sponsors have several opportunities to engage with PharmaCare over the course of a review.

>>> *To learn more, see Health Industry Professionals.*

CONFLICT OF INTEREST GUIDELINES

PharmaCare is committed to a fair, independent, objective, and unbiased drug review process. All the individuals who take part in the review of a drug submission, including members of the DBC, the DRRC, and the DRRTs, are held to the highest ethical standards.

For this reason, each person involved in the drug review process must declare any relationship they, or their immediate family, have that creates—or could appear to create – a conflict of interest[6]. The need to disclose conflict of interest information is an ongoing responsibility for all individuals and organizations involved in the review process.

Examples of information that needs to be disclosed include: payments or research funds received from a company that may benefit from the drug coverage decision; financial ownership in such a company; being employed by such a company; and any arrangement or relationship through which the participant could either earn or lose money because of a Ministry drug coverage decision.

Whether or not an individual or organization is able to participate depends on the particular drug under review. As such, declaring a possible conflict of interest does not automatically exclude an individual or organization from participating in the drug review process.

>>> *To learn more, access the Ministry's Conflict of Interest Guidelines (PDF).*

[6] PharmaCare guidelines for the drug review process state that "a conflict of interest may exist whenever a Participant or an Immediate Family Member of a Participant has a direct or indirect interest or relationship, financial or otherwise, with an Entity that may affect or reasonably appear to affect the objectivity or fairness of the Participant in the Drug Benefit Review Process."

PHARMACARE DRUG REVIEW TIMELINES

PharmaCare starts its review process when the CDR drug review process is complete, (i.e., on the date the CDR final recommendation and reasons for recommendation are issued).

All other patented drug submission reviews start on the date PharmaCare received the complete submission.

PharmaCare has set specific target timelines for completing drug reviews. The target timeline for a drug coverage decision (that is, time-to-listing decision) is defined as the time from which the Ministry begins its review to the time that the PharmaCare drug decision comes into effect. This usually includes completing all implementation steps.

Most drug submissions undergo a **standard review,** which has a target timeline of nine months, or a **complex review** with a target timeline of twelve months. A complex review usually involves more steps, such as developing clinical criteria for coverage and/or a Special Authority form, and completing discussions with a drug manufacturer (including national negotiations through pCPA).

>>> To learn more about the review periods for recently reviewed patented drugs, see the Quarterly Report on Drug Submission Reviews (PDF).

PRIORITY REVIEWS

A drug submission may be given priority status if it:

- meets a significant unmet clinical need and shows major therapeutic benefit; or
- shows substantial economic benefit.

A priority review has a six-month target timeline for standard submissions, and a nine-month target timeline for complex submissions.

FURTHER INFORMATION

You can find more information about drug reviews and drug review results on the PharmaCare website. See:

- Health Industry Professionals
- Submitting Patented Drugs and Biosimilars
- Conflict of Interest Guidelines (PDF)
- Drug Review Decisions